An animal model of MYC-driven medulloblastoma.

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Public Summary:
Medulloblastoma is the most common malignant brain tumor in children. Patients whose tumors have high levels of a gene called Myc usually have an extremely poor prognosis, but until recently there have been no animal models of this subtype of the disease. We have now shown that cerebellar stem cells engineered to express Myc, coupled with a mutated form of a second gene (p53), form aggressive tumors following transplantation. These tumors resemble human MYC-driven medulloblastoma both histologically and at a molecular level. Notably, we have found that antagonists of the intracellular enzyme PI 3-kinase can inhibit the growth of MYC-driven medulloblastoma cells in vitro and in vivo. The stem cell-based models we have created will allow us to study the biology of MYC-driven medulloblastoma and to test drugs that may be useful for treating the disease.

Scientific Abstract:
Medulloblastoma (MB) is the most common malignant brain tumor in children. Patients whose tumors exhibit overexpression or amplification of the MYC oncogene (c-MYC) usually have an extremely poor prognosis, but there are no animal models of this subtype of the disease. Here, we show that cerebellar stem cells expressing Myc and mutant Trp53 (p53) generate aggressive tumors following orthotopic transplantation. These tumors consist of large, pleiomorphic cells and resemble human MYC-driven MB at a molecular level. Notably, antagonists of PI3K/mTOR signaling, but not Hedgehog signaling, inhibit growth of tumor cells. These findings suggest that cerebellar stem cells can give rise to MYC-driven MB and identify a novel model that can be used to test therapies for this devastating disease.